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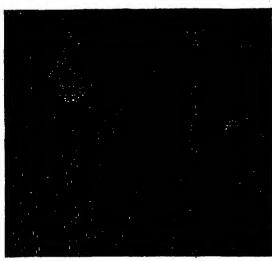
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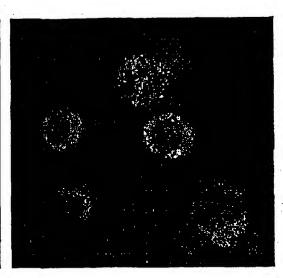
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(57) Abstract

An improved delivery system for antisense oligonucleotides involves a liposomal composition, comprising a liposome which consists essentially of neutral phospholipids and an antisense oligonucleotide that is entrapped in the liposome and is selected from the group consisting of phosphodiester oligonucleotides, phosphorothioate oligonucleotides, and p-ethoxy oligonucleotides.

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C. DOCUM	IENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the r	elevant passages	Relevant to claim No.
Х	DE 41 10 085 A (BOEHRINGER INGELINTERNATIONAL GMBH) 1 October 199 see page 2, line 65 - page 3, line see page 23, line 37 - line 48	92 /	1,2
Υ	WO 95 03788 A (BOARD OF REGENTS, UNIVERSITY OF TEXAS SYSTEM) 9 Fel 1995 see page 8, line 8 - page 11, li	bruary	1-4,6, 10-12
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(Continu	tion) DOCUMENTS CONSIDERED TO BE RELEVANT	
ategory *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	NUCLEIC ACIDS RESEARCH, vol. 19, no. 20, 25 October 1991, EYNSHAM ,OXFORD (GB), pages 5551-5559, XP002027215 S. AKHTAR ET AL.: "interactions of antisense DNA oligonucleotide analogs with phospholipid membranes (liposomes) " see the whole document see page 5553; table 1	1-4,6, 10-12
•	SCIENCE, vol. 261, no. 5124, 20 August 1993, WASHINGTON (US), pages 1004-1012, XP002027216 C.A. STEIN ET AL.: "antisense oligonucleotides as therapeutic agents-is the bullet really magical" see page 1005, column 1; figure 1	1-4,6, 10-12
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International application No

PCT/US 96/14146

Box ! Observations where certain claums were found unsearchable (Continuation of item 1 of first sheet)	
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
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	1
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Information on patent family members

PCT/US 96/14146

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 4110085 A	01-10-92	NONE	
WD 9503788 A	09-02-95	US 5417978 A AU 7407994 A CA 2168243 A EP 0711149 A JP 9501160 T	23-05-95 28-02-95 09-02-95 15-05-96 04-02-97